SUPPLEMENTARY INFORMATION

Histamine deficiency promotes inflammation-associated carcinogenesis through reduced myeloid maturation and accumulation of $CD11b^{+}Ly6G^{+}$ immature myeloid cells

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Supplementary Tables 1-4

Legends for supplementary Tables 1- 4

Differentially expressed genes of $CD11b^+Gr\text{-}1^+$ IMCs were examined by microarray (Affymetrix Mouse 430.2 array). Total RNA of Hdc-expressing $CD11b^+Gr\text{-}1^+$ IMCs of bone marrow were extracted from *Hdc*-EGFP and *Hdc*-EGFP/$Hdc^{-/-}$ mice (3 mice in each group). $CD11b^+Gr\text{-}1^+$ MDSCs from colonic tumors were sorted from 10-12 tumors from WT and $Hdc^{-/-}$ mice (5 mice in each group) and pooled to extract total RNA for Microarray studies. Four sets of comparisons were performed to screen the upregulated or downregulated genes in the $CD11b^+Gr\text{-}1^+$ IMCs or MDSCs (experiment group) from $Hdc^{-/-}$ versus WT mice. Set 1: *Hdc*-expressing $CD11b^+Gr\text{-}1^+$ IMCs from the bone marrow of $Hdc^{-/-}$ mice compared to bone marrow-derived IMCs of WT mice. Set 2: $CD11b^+Gr\text{-}1^+$ MDSCs from tumors of $Hdc^{-/-}$ mice compared to MDSCs from WT mice. Set 3: $CD11b^+Gr\text{-}1^+$ MDSCs of WT colonic tumors compared to IMCs in WT bone marrow. Set 4: $CD11b^+Gr\text{-}1^+$ MDSCs of colonic tumors from $Hdc^{-/-}$ mice compared to IMCs from the bone marrow of $Hdc^{-/-}$ mice. Table 1. Upregulated (abundant) genes of inflammatory cytokines and receptors in $Hdc^{-/-}$ mice. Table 2. Upregulated (abundant) genes of chemokines and chemokine receptors in $Hdc^{-/-}$ mice. Table 3. Upregulated (abundant) genes of adhesion molecule genes in $Hdc^{-/-}$ mice. Table 4. Upregulated (abundant) DNA methylation related genes in $Hdc^{-/-}$ mice.

Supplementary Table. 1

Microarray data (1): Inflammatory cytokines and receptors

a

Control 1	$CD11b^+Gr\text{-}1^+$ IMCs of WT bone marrow	
Experiment 1 (genes MORE abundant)	$CD11b^+Gr\text{-}1^+$ MDSCs of *Hdc*$^{-/-}$ bone marrow	
Log2 Ratio	Gene Symbol	Gene Description
1.34	IL-7 R	interleukin 7 receptor
0.62	IL-1	interleukin 1 family,
0.59	IL-17 RA	interleukin 17 receptor A
0.59	IL-18 bp	interleukin 18 binding protein
0.38	IL-6 R	interleukin 6 receptor, alpha
0.22	IL-18	interleukin 18

b

Control 2	$CD11b^+Gr\text{-}1^+$ IMCs of WT colon tumor	
Experiment 2 (genes MORE abundant)	$CD11b^+Gr\text{-}1^+$ MDSCs of *Hdc*$^{-/-}$ colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
2.59	IL-18	interleukin 18
1.65	IL-1RAP	interleukin 1 receptor accessory protein
1.56	IL-17 R-c	interleukin 17 receptor C
1.28	IL-15	interleukin 15
1.28	IL-13 R	interleukin 13 receptor, alpha
1.26	IL-10 R	interleukin 10 receptor, alpha
0.93	IL-17 R-a	interleukin 17 receptor A
0.75	IL-6 R-a	interleukin 6 receptor, alpha

c

Control 3	$CD11b^+Gr\text{-}1^+$ IMCs of WT bone marrow	
Experiment 3 (genes MORE abundant)	$CD11b^+Gr\text{-}1^+$ MDSCs of WT colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
9.01	IL-1α	interleukin 1 alpha
8.02	IL-6	interleukin 6
2.97	IL-7 R	interleukin 7 receptor
2.52	IL-1β	interleukin 1 beta
2.51	IL-10 R	interleukin 10 receptor, alpha
2.38	IL-13 R	interleukin 13 receptor, alpha
1.96	IL-18	interleukin 18
1.72	IL-10	interleukin 10
1.07	IL-4 R	interleukin 4 receptor, alpha
0.13	IL-18 RAP	interleukin 18 receptor accessory protein

d

Control 4	$CD11b^+Gr\text{-}1^+$ IMCs of *Hdc*$^{-/-}$ bone marrow	
Experiment 4 (genes MORE abundant)	$CD11b^+Gr\text{-}1^+$ MDSCs of *Hdc*$^{-/-}$ colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
8.55	IL-1α	interleukin 1 alpha
8.54	IL-6	interleukin 6
5.78	IL-10 R	interleukin 10 receptor, alpha
4.35	IL-13 R	interleukin 13 receptor, alpha
4.33	IL-18	interleukin 18
3.7	IL-1β	interleukin 1 beta
3.08	IL-23 R	interleukin 23, alpha subunit p19
2.49	IL-1RAP	interleukin 1 receptor accessory protein
2.39	Il-4 R	interleukin 4 receptor, alpha
2.32	IL-7 R	interleukin 7 receptor
1.79	IL-17 R-c	interleukin 17 receptor C
1.72	IL-10	interleukin 10
1.29	IL-1 R II	interleukin 1 receptor, type II

Table 1. Upregulated (abundant) genes of inflammatory cytokines and receptors in *Hdc*$^{-/-}$ mice.

Supplementary Table. 2

Microarray data (2): Chemokines and chemokine receptors

a

Control 1	CD11b^{+}Gr-1^{+} IMCs of WT bone marrow	
Experiment 1 (genes MORE abundant)	CD11b^{+}Gr-1^{+} MDSCs of *Hdc*$^{-/-}$ bone marrow	
Log2 Ratio	Gene Symbol	Gene Description
0.76	CCR-2	chemokine (C-C motif) receptor 2
0.48	CXCR-4	chemokine (C-X-C motif) receptor 4
0.45	CCR-4	chemokine (C-C motif) receptor 4
0.36	CXCL-5	chemokine (C-X-C motif) ligand 5

b

Control 2	CD11b^{+}Gr-1^{+} IMCs of WT colon tumor	
Experiment 2 (genes MORE abundant)	CD11b^{+}Gr-1^{+} MDSCs of *Hdc*$^{-/-}$ colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
4.78	CCL-5	chemokine (C-C motif) ligand 5
4.27	CCR-3	chemokine (C-C motif) receptor 3
2.83	CCR-9	chemokine (C-C motif) receptor 9
2.19	CCR-2	chemokine (C-C motif) receptor 2
2.05	CCR-6	chemokine (C-C motif) receptor 6
2.03	CCL-28	chemokine (C-C motif) ligand 28
1.12	CXCL-5	chemokine (C-X-C motif) ligand 5
0.99	CXCR-3	chemokine (C-X-C motif) receptor 3
0.97	CCL-6	chemokine (C-C motif) ligand 6
0.9	CCL-9	chemokine (C-C motif) ligand 9
0.83	CXCL-10	chemokine (C-X-C motif) ligand 10

c

Control 3	CD11b^{+}Gr-1^{+} IMCs of WT bone marrow	
Experiment 3 (genes MORE abundant)	CD11b^{+}Gr-1^{+} MDSCs of WT colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
8.94	CXCL-1	chemokine (C-X-C motif) ligand 1
8.44	CXCL-3	chemokine (C-X-C motif) ligand 3
7.52	CCRl2	chemokine (C-C motif) receptor-like 2
6.31	CXCL-2	chemokine (C-X-C motif) ligand 2
5.92	CCL-24	chemokine (C-C motif) ligand 24
5.88	CCL-4	chemokine (C-C motif) ligand 4
5.76	CCR-5	chemokine (C-C motif) receptor 5
4.46	CCR-2	chemokine (C-C motif) receptor 2
4.44	CCL-8	chemokine (C-C motif) ligand 8
3.25	CCL-12	chemokine (C-C motif) ligand 12
2.43	CCL-9	chemokine (C-C motif) ligand 9
2.42	CXCL-5	chemokine (C-X-C motif) ligand 5
2.12	CCL-2	chemokine (C-C motif) ligand 2
1.81	CCL-5	chemokine (C-C motif) ligand 5

d

Control 4	CD11b^{+}Gr-1^{+} IMCs of *Hdc*$^{-/-}$ bone marrow	
Experiment 4 (genes MORE abundant)	CD11b^{+}Gr-1^{+} MDSCs of *Hdc*$^{-/-}$ colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
10.92	CXCL-2	chemokine (C-X-C motif) ligand 2
10.58	CXCL-3	chemokine (C-X-C motif) ligand 3
9.92	CCL-3	chemokine (C-C motif) ligand 3
8.82	CCRl2	chemokine (C-C motif) receptor-like 2
8.44	CXCL-1	chemokine (C-X-C motif) ligand 1
6.57	CCL-24	chemokine (C-C motif) ligand 24
6.32	CCL-4	chemokine (C-C motif) ligand 4
5.84	CCR-2	chemokine (C-C motif) receptor 2
5.61	CCR-5	chemokine (C-C motif) receptor 5
5.21	CCR-3	chemokine (C-C motif) receptor 3
4.63	CCL-8	chemokine (C-C motif) ligand 8
4.55	CXCL-9	chemokine (C-X-C motif) ligand 9
3.18	CXCL-5	chemokine (C-X-C motif) ligand 5
3.01	CCR-9	chemokine (C-C motif) receptor 9
2.84	CXCL-13	chemokine (C-X-C motif) ligand 13

Table 2. Upregulated (abundant) genes of chemokines and chemokine receptors in *Hdc*$^{-/-}$ mice.

Supplementary Table. 3

Microarray data (3): Adhesive molecules

a

Control 1	CD11b$^+$Gr-1$^+$ IMCs of WT bone marrow	
Experiment 1 (genes MORE abundant)	CD11b$^+$Gr-1$^+$ MDSCs of *Hdc*$^{-/-}$ bone marrow	
Log2 Ratio	Gene Symbol	Gene Description
0.89	CD44	CD44 antigen
0.38	ICAM-2	intercellular adhesion molecule 2
0.37	CAM-1	cell adhesion molecule 1

b

Control 2	CD11b$^+$Gr-1$^+$ IMCs of WT colon tumor	
Experiment 2 (genes MORE abundant)	CD11b$^+$Gr-1$^+$ MDSCs of *Hdc*$^{-/-}$ colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
1.76	ICAM-1	intercellular adhesion molecule 1
1.07	VCAM-1	vascular cell adhesion molecule 1
0.94	CAM-1	cell adhesion molecule 1
0.79	ALCAM	activated leukocyte cell adhesion molecule
0.59	P-selectin	selectin, platelet (p-selectin) ligand
0.51	CD44	CD44 antigen, mRNA
0.25	ICAM-2	intercellular adhesion molecule 2

c

Control 3	CD11b$^+$Gr-1$^+$ IMCs of WT bone marrow	
Experiment 3 (genes MORE abundant)	CD11b$^+$Gr-1$^+$ MDSCs of WT colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
4.71	ICAM-1	intercellular adhesion molecule 1
0.57	VCAM-1	vascular cell adhesion molecule 1
0.51	CAM-1	cell adhesion molecule 1
0.1	CD44	CD44 antigen, mRNA
0.07	E-selectin	selectin, endothelial cell

d

Control 4	CD11b$^+$Gr-1$^+$ IMCs of *Hdc*$^{-/-}$ bone marrow	
Experiment 4 (genes MORE abundant)	CD11b$^+$Gr-1$^+$ MDSCs of *Hdc*$^{-/-}$ colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
6.71	ICAM-1	intercellular adhesion molecule 1
4.02	VCAM-1	vascular cell adhesion molecule 1
1.35	CAM-1	cell adhesion molecule 1
0.78	CD44	CD44 antigen, mRNA
0.44	P-selectin	selectin, platelet (p-selectin) ligand
0.37	PE-CAM-1	platelet/endothelial cell adhesion molecule 1

Table 3. Upregulated (abundant) genes of adhesion molecule genes in *Hdc*$^{-/-}$ mice.

Supplementary Table. 4

Microarray data (4): Methylation related genes

a

Control 1	CD11b$^+$Gr-1$^+$ IMCs of WT bone marrow	
Experiment 1 (genes MORE abundant)	CD11b$^+$Gr-1$^+$ MDSCs of *Hdc*$^{-/-}$ bone marrow	
Log2 Ratio	Gene Symbol	Gene Description
0.38	Prmt5	protein arginine N-methyltransferase 5
0.37	Mtap	methylthioadenosine phosphorylase
0.34	Mettl3	methyltransferase like 3
0.28	As3mt	arsenic (+3 oxidation state) methyltransferase

b

Control 2	CD11b$^+$Gr-1$^+$ IMCs of WT colon tumor	
Experiment 2 (genes MORE abundant)	CD11b$^+$Gr-1$^+$ MDSCs of *Hdc*$^{-/-}$ colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
5.2	Mettl 7B	methyltransferase like 7B
2.08	Mettl 7A1	methyltransferase like 7A1
1.8	Comt 1	catechol-O-methyltransferase 1
1.54	Mtap	methylthioadenosine phosphorylase
1.20	Prmt 2	protein arginine N-methyltransferase 3
1.12	Prmt 7	protein arginine N-methyltransferase 7
1.01	Prmt 3	protein arginine N-methyltransferase 3
0.98	Dnmt3A	DNA methyltransferase 3A
0.72	Dnmt3B	DNA methyltransferase 3B
0.69	Mecp2	methyl CpG binding protein 2

c

Control 3	CD11b$^+$Gr-1$^+$ IMCs of WT bone marrow	
Experiment 3 (genes MORE abundant)	CD11b$^+$Gr-1$^+$ MDSCs of WT colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
2.02	As3mt	arsenic (+3 oxidation state) methyltransferase
1.15	Comt 1	catechol-O-methyltransferase 1
0.93	Prmt 2	protein arginine N-methyltransferase 2
0.84	Mtap	methylthioadenosine phosphorylase
0.69	Mettl 7B	methyltransferase like 7B

d

Control 4	CD11b$^+$Gr-1$^+$ IMCs of *Hdc*$^{-/-}$ bone marrow	
Experiment 4 (genes MORE abundant)	CD11b$^+$Gr-1$^+$ MDSCs of *Hdc*$^{-/-}$ colon tumor	
Log2 Ratio	Gene Symbol	Gene Description
5.69	Mettl 7B	methyltransferase like 7B
3.06	Comt 1	catechol-O-methyltransferase 1
2.46	Mthfr	5,10-methylenetetrahydrofolate reductase
2.38	Mtap	methylthioadenosine phosphorylase
2.19	Prmt 2	protein arginine N-methyltransferase 3
1.85	As3mt	arsenic (+3 oxidation state) methyltransferase
1.07	Prmt 7	protein arginine N-methyltransferase 7
1.02	Prmt 3	protein arginine N-methyltransferase 3
0.82	Mecp2	methyl CpG binding protein 2

Table 4. Upregulated (abundant) DNA methylation related genes in *Hdc*$^{-/-}$ mice.